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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/533,942	05/04/2005	Enrico Garaci	725.1046	9693

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EXAMINER	
ZAREK, PAUL E	

ART UNIT	PAPER NUMBER
1628	

NOTIFICATION DATE	DELIVERY MODE
11/26/2010	ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

info@lmiplaw.com

Office Action Summary	Application No.	Applicant(s)	
	10/533,942	GARACI ET AL.	
	Examiner	Art Unit	
	Paul Zarek	1628	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *18 May 2010*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *4-9 and 13-18* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *4-9 and 13-18* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Continued Examination Under 37 CFR 1.114

1. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 05/18/2010 has been entered.

Status of the Claims

2. Claims 4, 7, 13, and 16 have been amended by the Applicant in correspondence filed on 05/18/2010. Claims 4-7 and 13-18 are currently pending. This is the first Office Action on the merits of the claim(s) following the second request for continued examination.

RESPONSE TO ARGUMENTS

3. Claims 4-9 and 13-18 were rejected under 35 U.S.C. 103(a) as being unpatentable over Root, et al. (Journal of General Virology, 2000), in view of Stewart, et al. (Biochemistry, 1999), and Heredia, et al. (Journal of Acquired Immune Deficiency Syndromes, 2000). Applicants traversed this rejection on the grounds that the combination of prior art does not teach or fairly suggest the claimed invention. Specifically, Applicants contend that the art do not disclose a method of inhibiting influenza virus replication or treating an influenza virus infection comprising administration of resveratrol in a dose that inhibits viral cell replication but does not

inhibit target cell entry by the virus. Applicants contend that Root, et al., disclose only that a PKC inhibitor blocks influenza virus entry to a cell, but does not show that the PKC inhibitor (bisindolylmaleimide 1.HCl) affects viral cell replication once the virus enters the cell. Applicants submit that nothing in Stewart, et al., or Heredia, et al., compensate for the alleged deficiencies in Root, et al. Examiner notes that Applicants have not disagreed with Stewart, et al., or Heredia, et al., in the capacity in which they were applied to the instant claims (e.g. that resveratrol inhibits PKC [Stewart, et al.] or the virtues of resveratrol (i.e. low cost, established safety profile) [Heredia, et al.]). Respectfully, Examiner does not find Applicants' arguments persuasive.

4. Applicants appear to be the first to discover that resveratrol can inhibit influenza virus replication by inhibiting PKC, thereby structurally interfering with a functional cell structure of the virus. However, recognition of additional properties does not render nonobvious an otherwise known invention (*In re Wiseman*, 596 F.2d 1019, 201 USPQ 658 (CCPA 1979); MPEP § 2145(II)). Root, et al., teaches that PKC can inhibit influenza virus replication by inhibiting entry of the virus into a target cell. Stewart, et al., note that resveratrol is a PKC inhibitor and Heredia, et al., provide motivation to use resveratrol rather than another compound. Based on this combination of prior art, the artisan would reasonably predict that full or significant inhibition of PKC would be sufficient to inhibit influenza virus replication and to treat influenza virus infection. In the absence of a specific teaching in the art, the artisan would be guided to use a dose of resveratrol known to inhibit PKC. Stewart, et al., disclose that resveratrol "potently inhibits" cellular PKC at a concentration of 15 μM (pg 13249, col 2, para 1, lines 4-5). This dose corresponds to 3.4 μg/mL. (Resveratrol molecular weight: 228.24 g/mol;

15 μmol/1000 mL x 228.24 g/mol = 3423.6 μg/1000 mL = 3.4236 μg/mL.) Thus, a dose of 3.4 μg/mL is a reasonable starting point to inhibit influenza virus replication and/or treat influenza virus infection.

5. The instant specification uses 10-20 μg/mL resveratrol in the mouse models of influenza infection (pg 14-16; Example). Applicants' *in vitro* data shows that 20 μg/mL is sufficient to inhibit influenza virus replication without affecting the virus's ability to enter the cell. So, when the artisan administers 3.4 μg/mL of resveratrol to inhibit influenza virus replication, he or she would assume that such a dose prevents the virus from entering the cell. Applicants' data show, however, that such a dose is effective because it disrupts the functional cell structure of the virus. Thus, the dose of resveratrol that the art suggests using to inhibit influenza virus replication is a dose that does not inhibit viral entry into the target cell. Therefore, the rejection of Claims 4-9 and 13-18 under 35 U.S.C. 103(a) as being unpatentable over Root, et al., in view of Stewart, et al., and Heredia, et al., is maintained.

6. Below are listed new grounds of rejection that are not necessitated by amendment to the claims. Therefore, this office action is considered **non-final.**

Claim Rejections - 35 USC § 112 (1st paragraph)

7. The text of Title 35, U.S.C. § 112, first paragraph, can be found in a prior Office action.

8. Claims 4-9 and 13-18 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the

relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. Independent Claims 4, 7, 13, and 16, from which all other claims depend, were amended to limit the dose of resveratrol to a dose that does not inhibit influenza virus target cell entry. This is considered new matter because the originally filed disclosure does not explicitly or implicitly disclose that only specific doses of resveratrol meet this limitation.

9. The experiments disclosed on pgs 8 and 9 utilize 20 μg/mL resveratrol to determine that the compound does not affect influenza virus entry into a target cell. However, there is no discussion in the specification indicating that this phenomenon is relevant only to 20 μg/mL of resveratrol. Likewise, the *in vivo* experiment (pgs 14-16) use 20 μg/mL based on the *in vitro* data. There is no discussion regarding which doses of resveratrol are required to inhibit influenza virus replication yet do not inhibit the entry of the virus into a target cell.

Conclusion

10. Claims 4-9 and 13-18 remain rejected.

11. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Paul Zarek whose telephone number is (571) 270-5754. The examiner can normally be reached on Monday-Thursday, 7:30-5:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Brandon Fetterolf can be reached on (571) 272-2919. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

PEZ

/San-ming Hui/
Primary Examiner, Art Unit 1628